

## General

### Guideline Title

Follow-up of patients who are clinically disease-free after primary treatment for fallopian tube, primary peritoneal, and epithelial ovarian cancer.

### Bibliographic Source(s)

Le T, Kennedy EB, Dodge J, Elit L, Ovarian Follow-up Guideline Expert Panel. Follow-up of patients who are clinically disease-free after primary treatment for fallopian tube, primary peritoneal, and epithelial ovarian cancer. Toronto (ON): Cancer Care Ontario (CCO); 2015 Nov 11. 34 p. (Program in Evidence-based Care Guideline; no. 4-22). [27 references]

### Guideline Status

This is the current release of the guideline.

The Program in Evidence-based Care guideline, initially the full original Guideline, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the [Cancer Care Ontario \(CCO\) Web site](#)  for details on any new evidence that has emerged and implications to the guidelines.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Recommendations

### Major Recommendations

Note from the National Guideline Clearinghouse (NGC): The authors of this guideline endorsed recommendations from the Cancer Australia guidance document entitled *Follow-up of Women with Epithelial Ovarian Cancer: A Systematic Review*. The Working Group members identified key recommendations from that document, which are reproduced verbatim.

1. Recommendations for Follow-up Post-treatment
  - a. While the optimal method of follow-up is not yet established, possible options for follow-up and the implications and possible consequences of these options should be discussed with the woman at the completion of primary treatment.
  - b. Consideration should be given as to how anxiety might be lessened, such as scheduling tests before the visit so that test results are available for discussion at the time of the follow-up visit.
2. Recommendations for Cancer Antigen 125 (CA-125) in Follow-up
  - a. Women should be informed that there is no evidence that monitoring CA-125 improves survival outcome, and that it may worsen quality of life. There should be a time provided for the woman and her clinician to discuss the implications of monitoring progress and initiating treatment based on CA-125 levels. Women can be advised that they have the option to have CA-125 levels tested at agreed intervals, or not at all. Women who choose to have CA-125 levels measured should be informed that CA-125 levels may

fluctuate due to individual and laboratory assay variations, and the implications of stable, fluctuating, and rising levels should be discussed.

- b. Women should be fully informed of the limitations and potential harms of routine measurement of CA-125 during follow-up and supported to make an informed decision, considering the findings of the randomized controlled trial (RCT) on follow-up after ovarian cancer.
- c. The decision to initiate re-treatment requires careful consideration based on the individual woman's situation, and factors including the nature of the recurrence and the wishes of the woman.

### 3. Recommendations for Timing of Follow-up Consultations

- a. Women should be offered the opportunity to have regular follow-up. Discussion with the woman about follow-up could incorporate a schedule of follow-up appointments, including the possibility of no formal follow-up schedule, based on the identified needs and wishes of the individual.
- b. There is no recommended frequency of follow-up consultations, but a clear and mutually agreed arrangement should be negotiated with the women, tailored according to risk and to individual patient characteristics, which acknowledges the benefits of an ongoing relationship and the opportunity to deal with issues as they arise.
- c. Women residing in rural and regional areas face additional challenges of access to specialist clinicians for follow-up appointments. Individual circumstances should be considered when establishing a follow-up schedule.

### 4. Recommendations for Format for Follow-up Consultations

- a. The basic format of consultation is to update the patient history, assess psychosocial and supportive care needs, and undertake physical examination, which may include pelvic examination.
- b. Women should be encouraged to report a range of symptoms, including nausea, vomiting, abdominal distension, cramping, pain, and shortness of breath, and any other concerning symptoms.
- c. Radiological imaging should not be done routinely, but should be performed if there is clinical or CA-125 evidence of recurrence. The rationale for not undertaking routine imaging should be discussed with the woman.

### 5. Recommendation for Models of Follow-up Care

- a. A woman may be reviewed by either a gynecologic oncologist or a medical oncologist. Communication with a woman's primary care physician should be maintained throughout follow-up.
- b. The use of alternate models of care for women with ovarian cancer, such as primary care physician or nurse-led follow-up, telephone follow-up and patient-initiated care is an area for future research. Some of the issues that would need to be addressed in any future studies include patient and clinician preferences, the effectiveness and cost effectiveness of the alternative models, and the ability of health services to support them.

## Clinical Algorithm(s)

None provided

## Scope

## Disease/Condition(s)

Fallopian tube, primary peritoneal, and epithelial ovarian cancer

## Guideline Category

Evaluation

Management

## Clinical Specialty

Obstetrics and Gynecology

## Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

## Guideline Objective(s)

To make recommendations for appropriate follow-up of women with confirmation of remission, after surgery and first-line chemotherapy, for fallopian tube, primary peritoneal, or epithelial ovarian cancer

## Target Population

Women who have received confirmation of clinical complete remission (i.e., are disease-free) after surgery and first-line chemotherapy for fallopian tube, primary peritoneal, or epithelial ovarian cancer

Note: Disease-free status is determined according to the standard procedure at the unit where treatment was provided and may include negative clinical examinations, negative imaging investigations, and/or negative tumour marker results.

## Interventions and Practices Considered

1. Discussion of post-treatment follow-up options
2. Patient choice of cancer antigen-125 (CA-125) monitoring
3. Patient education on the limitations and harms of CA-125 measurement
4. Follow-up consultations
  - Timing based on patient risk factors and individual characteristics/need
  - Format to update patient history, assess psychosocial/supportive care needs, undertake physical examination/pelvic examination and symptom assessment
  - Imaging only if clinical or CA-125 evidence of recurrence
5. Models of follow-up care
  - Gynecologic oncologist or a medical oncologist
  - Communication with primary care physician

## Major Outcomes Considered

- Anxiety level associated with the time period before and after follow-up visits
- Overall survival rate
- Median survival time
- Quality of life
- Utility of follow-up methods

## Methodology

### Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

# Description of Methods Used to Collect/Select the Evidence

## Search for Existing Guidelines

A search for existing guidelines is generally undertaken prior to searching for existing systematic reviews or primary literature. This is done with the goal of identifying existing guidelines for adaptation or endorsement in order to avoid the duplication of guideline development efforts across jurisdictions. Only guidelines that are based on a systematic review of evidence are considered for inclusion; consensus-based guidelines are generally not considered. For this project, the following sources were searched for existing guidelines that addressed the research questions:

- National Guideline Clearinghouse (NGC)
- Guideline developer Web sites (Scottish Intercollegiate Guidelines Network, UK National Institute for Health and Care Excellence, American Society of Clinical Oncology)

Guidelines that were considered relevant to the objectives and the research questions were then evaluated for quality using the seven-item Rigour of Development Domain of the Appraisal of Guidelines Research and Evaluation II (AGREE II) instrument. A search for existing guidelines yielded an appropriate source document for endorsement.

The guideline, called *Follow-up of Women with Epithelial Ovarian Cancer*, was produced by Cancer Australia. It was based on a systematic review that received high scores for quality on the AMSTAR tool, and was current to January 2010. The members of the Working Group agreed that the Australian document would be suitable for endorsement, with potential modifications to suit the Ontario context, provided that no more recent evidence was available of a contradictory nature. Thus, the members of the Working Group decided to systematically search the literature from February 2010 onwards for any more current systematic reviews, and, if necessary, primary studies.

## Search for Systematic Reviews

MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews were searched for existing systematic reviews that had been published after the final search date (January 2010) of Cancer Australia's *Follow-up of Women with Epithelial Ovarian Cancer: A Systematic Review*. The search terms, which were adopted from Cancer Australia's systematic review, related to ovarian cancer and asymptomatic detection of recurrence and follow-up (see Appendix 3 in the original guideline document). This portion of the search was limited to review articles. Systematic reviews that were found to be directly relevant to this guideline were assessed using the AMSTAR (A Measurement Tool to Assess Systematic Reviews) tool.

## Search for Primary Literature

If a relevant systematic review was found, the Working Group would include the results of that review in the evidence base and conduct a search for primary literature from that review's final search date to the present. If no relevant systematic reviews were found, then the primary literature would be searched from the Cancer Australia guideline's search date (January 2010) to the present. MEDLINE and EMBASE were searched with the same terms related to ovarian neoplasms and follow-up used in the search for systematic reviews (see Appendix 3 in the original guideline document). Clinicaltrials.gov was searched for in-progress randomized controlled trials (RCTs).

## Study Selection Criteria and Process

In order to limit the review to the highest possible level of evidence, and in view of the fact that this literature search was intended to update an existing source of primary literature, publication types other than RCTs were not considered eligible for inclusion. There was no size limit specified for RCTs. Studies of follow-up of a suspected recurrence are not included in the scope of this report.

Articles were limited to those reported in the English language because resources for translation were not available. A review of the titles and abstracts that resulted from the search was conducted by the study methodologist.

# Number of Source Documents

## Existing Guidelines

The search for existing guidelines yielded an appropriate source document for endorsement.

## Primary Literature and Systematic Reviews

Two systematic reviews and no primary studies met the inclusion criteria. See Appendix 4 in the original guideline document for a PRISMA diagram of the search for primary literature and systematic reviews.

## Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

## Rating Scheme for the Strength of the Evidence

Not applicable

## Methods Used to Analyze the Evidence

Systematic Review

## Description of the Methods Used to Analyze the Evidence

### Synthesizing the Evidence

As the members of the Working Group were aware prior to the initiation of the search that the number of studies in this field is very limited, a meta-analysis was not planned.

## Methods Used to Formulate the Recommendations

Expert Consensus

## Description of Methods Used to Formulate the Recommendations

### Guideline Developers

This guideline was developed by the Ovarian Follow-up Guideline Development Group (GDG) (see Appendix 1 in the original guideline document), which was convened at the request of the Program in Evidence-based Care (PEBC) Gynecologic Cancer Disease Site Group (Gyne DSG).

The project was led by a small Working Group of the Ovarian Follow-up Guideline GDG, which was responsible for reviewing the evidence base, drafting the guideline recommendations, and responding to comments received during the document review process. The members of the Working Group had expertise in gynecologic oncology and health research methodology. Other members of the GDG served as the Expert Panel and were responsible for the review and approval of the draft document produced by the Working Group.

### Guideline Development Methods

The PEBC produces evidence-based and evidence-informed guidance documents using the methods of the Practice Guidelines Development Cycle. This process includes a systematic review, interpretation of the evidence, creation of draft recommendations by the members of the Working Group, internal review by content and methodology experts, and external review by Ontario clinicians and other stakeholders.

The PEBC uses the Appraisal of Guidelines Research and Evaluation II (AGREE II) framework as a methodological strategy for guideline development. AGREE II is a 23-item validated tool that is designed to assess the methodological rigour and transparency of guideline development.

The currency of each document is ensured through periodic review and evaluation of the scientific literature and, where appropriate, the addition of newer literature to the original evidence base. This is described in the PEBC Document Assessment and Review Protocol (see the "Availability of Companion Documents" field). PEBC guideline recommendations are based on clinical evidence, and not on feasibility of implementation; however, a list of implementation considerations such as costs, human resources, and unique requirements for special or disadvantaged populations

is provided along with the recommendations for information purposes. PEBC guideline development methods are described in more detail in the PEBC Handbook and the PEBC Methods Handbook (see the "Availability of Companion Documents" field).

#### Research Question

In women with confirmation of remission after surgery and first-line chemotherapy for epithelial ovarian cancer, what are the differences in survival rate, quality of life (QOL), and level of anxiety associated with different follow-up intervals and methods for detection of recurrence?

## Rating Scheme for the Strength of the Recommendations

Not applicable

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

External Peer Review

Internal Peer Review

## Description of Method of Guideline Validation

#### Guideline Review and Approval

Internal Review

For the guideline document to be approved, 75% of the content experts who comprise the Guideline Development Group (GDG) Expert Panel must cast a vote indicating whether or not they approve the document, or abstain from voting for a specified reason, and of those that vote, 75% must approve the document. In addition, the Program in Evidence-based Care (PEBC) Report Approval Panel (RAP), a three-person panel with methodology expertise, must unanimously approve the document. The Expert Panel and RAP members may specify that approval is conditional, and that changes to the document are required. If substantial changes are subsequently made to the recommendations during external review, then the revised draft must be resubmitted for approval by the RAP and the GDG Expert Panel.

External Review

Feedback on the approved draft guideline is obtained from content experts and the target users through two processes. Through the Targeted Peer Review, several individuals with content expertise are identified by the GDG and asked to review and provide feedback on the guideline document. Through Professional Consultation, relevant care providers and other potential users of the guideline are contacted and asked to provide feedback on the guideline recommendations through a brief online survey. This consultation is intended to facilitate the dissemination of the final guidance report to Ontario practitioners.

See Section 5 in the original guideline document for further discussion of the internal and external guideline review process and results.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The recommendations are supported by a clinical guideline and systematic reviews.

## Benefits/Harms of Implementing the Guideline Recommendations

## Potential Benefits

The greatest benefit of ongoing follow-up is the maintenance of a relationship with the oncologist and the reassurance associated with continued involvement in the cancer care system, given the high likelihood of recurrence. Other potential benefits include the opportunity to discuss ongoing psychosocial concerns and referral to appropriate providers, such as psychologists, psychiatrists, or social workers, reassurance or alleviation of anxiety after negative results at follow-up appointments, prompt identification of women who may be candidates for open clinical trials, and the opportunity to discuss importance of genetic testing and familial counselling.

## Potential Harms

- The Working Group members identified several harms that are associated with routine surveillance, including a potentially shorter time living in a progression-free status with no corresponding increase in overall survival time and a decrease in quality of life due to earlier initiation of treatment, anxiety associated with follow-up, inconvenience and cost of attending follow-up appointments, and potential for unnecessary and costly follow-up testing in the case of falsely elevated cancer antigen 125 (CA-125) levels.
- The Working Group members stress that if women opt not to engage in routine follow-up, they must be fully informed about signs and symptoms of recurrence, and be instructed to contact their oncologist or primary care provider if signs and symptoms suggestive of recurrence appear.

## Qualifying Statements

### Qualifying Statements

- Care has been taken in the preparation of the information contained in this report. Nevertheless, any person seeking to consult the report or apply its recommendations is expected to use independent medical judgment in the context of individual clinical circumstances or to seek out the supervision of a qualified clinician. Cancer Care Ontario (CCO) makes no representations or guarantees of any kind whatsoever regarding the report content or its use or application and disclaims any responsibility for its use or application in any way.
- The Working Group members stress that if women opt not to engage in routine follow-up, they must be fully informed about signs and symptoms of recurrence, and be instructed to contact their oncologist or primary care provider if signs and symptoms suggestive of recurrence appear.
- In some remote areas of Ontario, follow-up has been delivered via TeleHealth. This model of follow-up care for patients with ovarian cancer has not been studied; however, it may be a viable model for patients who live in geographically remote areas and who are not able to travel to a Cancer Centre.
- There are currently two ongoing randomized trials of secondary debulking surgery, DESKTOP III and GOG-0213 ([www.cancer.gov](http://www.cancer.gov) ). This guideline should be reviewed for currency when the results of these trials have been published.
- See the original guideline document for qualifying statements related to each specific recommendation.

## Implementation of the Guideline

### Description of Implementation Strategy

An implementation strategy was not provided.

### Implementation Tools

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents and Patient Resources* fields below.

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

## IOM Care Need

Getting Better

Living with Illness

## IOM Domain

Effectiveness

Patient-centeredness

## Identifying Information and Availability

### Bibliographic Source(s)

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### Adaptation

Not applicable: The guideline was not adapted from another source.

### Date Released

2015 Nov 11

### Guideline Developer(s)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

### Guideline Developer Comment

The Program in Evidence-based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario (CCO) and the Ontario Ministry of Health and Long-Term Care (OMHLTC).

### Source(s) of Funding

The Program in Evidence-based Care (PEBC) is a provincial initiative of Cancer Care Ontario (CCO) supported by the Ontario Ministry of Health and Long-Term Care (OMHLTC). All work produced by the PEBC is editorially independent from the OMHLTC.

### Guideline Committee



## Composition of Group That Authored the Guideline

*Authors:* T. Le, E.B. Kennedy, J. Dodge, L. Elit, Ovarian Follow-up Guideline Expert Panel

## Financial Disclosures/Conflicts of Interest

Conflict of interest declarations for all Guideline development Group (GDG) members are summarized in Appendix 1 of the original guideline, and were managed in accordance with the [Program in Evidence-based Care \(PEBC\) Conflict of Interest Policy](#) .

## Guideline Status

This is the current release of the guideline.

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Please visit the [Cancer Care Ontario \(CCO\) Web site](#)  for details on any new evidence that has emerged and implications to the guidelines.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Guideline Availability

Available from the [Cancer Care Ontario \(CCO\) Web site](#) .

## Availability of Companion Documents

The following are available:

- Follow-up of patients who are clinically disease-free after primary treatment for fallopian tube, primary peritoneal, and epithelial ovarian cancer. Summary. Toronto (ON): Cancer Care Ontario (CCO); 2015 Nov 21. 4 p. Available from the [Cancer Care Ontario \(CCO\) Web site](#) .
- Program in Evidence-based Care handbook. Toronto (ON): Cancer Care Ontario (CCO); 2012. 14 p. Available from the [CCO Web site](#) .
- Program in Evidence-based Care methods handbook. Toronto (ON): Cancer Care Ontario (CCO); 2014 Sep 23. Available from the [Program in Evidence-based Care \(PEBC\) Toolkit Web site](#) .
- Program in Evidence-based Care document assessment and review protocol. Toronto (ON): Cancer Care Ontario (CCO); 2015 Apr 16. 13 p. Available from the [CCO Web site](#) .

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI Institute on April 4, 2016.

## Copyright Statement

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## Disclaimer

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